WE CLAIM

1. A viral vector comprising an E2F responsive transcriptional nucleotide regulatory site that controls the expression of a viral gene.

2. A viral vector as described in claim 1 wherein said viral gene is an immediate early gene.

3. A viral vector as described in claim 2 wherein said viral vector is adenovirus.

4. A viral vector as described in claim 3, wherein said transcriptional nucleotide regulatory site is a promoter.

5. A viral vector as described in claim 4, wherein said E2F responsive promoter is substituted for an endogenous adenoviral E1a promoter.

6. A viral vector as described in claim 4, wherein said E2F responsive promoter is substituted for an endogenous adenoviral E4 promoter.

7. A viral vector as described in claim 6, wherein said viral vector further comprises nucleotide regulatory sites that substantially facilitate viral replication comprising Sp1, ATF, NF1 and NFIII/Oct-1.

8. A viral vector comprising a viral transcriptional nucleotide regulatory site that controls the expression of a viral gene, wherein said site is inactivated by the insertion of an E2F responsive transcriptional nucleotide regulatory site such that said E2F responsive transcriptional nucleotide regulatory site controls the expression of said viral gene.

9. A viral vector as described in claim 8 wherein said viral gene is an immediate early gene.

10. A viral vector as described in claim 9 wherein said viral vector is adenovirus.

11. A viral vector as described in claim 10, wherein said inactivated transcriptional nucleotide regulatory site is a promoter.

12. A viral vector as described in claim 11, wherein said inactivated transcriptional nucleotide regulatory site is an endogenous adenoviral E1a promoter.

13. A viral vector as described in claim 11, wherein said inactivated transcriptional nucleotide regulatory site is an endogenous adenoviral E4 promoter.

14. A viral vector as described in claim 11, wherein said inactivated transcriptional nucleotide regulatory site comprises both an endogenous adenoviral E1a and E4 promoters.

15. An viral vector as described in claims 1 or 8, wherein said transcriptional nucleotide regulatory sequence that is E2F responsive is human E2F-1.

16. A method for killing cancer cells in a population of cancer and normal cells with substantially no killing of said normal cells, comprising the steps of: contacting under infective conditions (1) a viral vector as described in claims 1 or 8 with (2) a cell population comprising said cancer and normal cells, and allowing sufficient time for said virus to infect said cell population.

17. A viral vector as described in claim1, wherein said viral vector is an adenoviral vector, and further comprising a heterologous gene.

18. A viral vector as described in claim 17, wherein said heterologous gene is inserted in a region of the adenoviral genome that is expressed late during the replication phase of said viral vector.

19. A viral vector as described in claim 18, wherein said heterologous gene is inserted in the E3b region of the virus.

20. A viral vector as described in claim 19, wherein said heterologous gene expression is under the control of adenoviral endogenous gene expression machinery.

21. A method for treating cancer in a patient in need of said treatment, comprising administering to said patient a viral vector as described in claim 20.

22. A method as described in claim 21 wherein said heterologous gene encodes a protein with anti-cancer activity.

23. A method as described in claim 22 wherein said heterologous gene encodes a protein selected from the group having biological activity consisting of immunomodulatory, pro-drug activator, apoptosis inducing, or chemotatic.

24. A method for sustained expression of a heterologous gene from an adenoviral vector, comprising contacting cancer cells with said adenoviral vector, wherein said adenoviral vector expresses said heterologous gene late during the adenoviral replication cycle.

25. A method as described in claim 24 wherein said late heterologous gene expression is under the control of adenoviral endogenous gene expression machinery.

26. A method as described in claim 25 wherein said late heterologous gene expression is under the control of endogenous gene expression machinery of the E3 region of adenovirus.

27. A nucleotide sequence that regulates the expression of an adenoviral early gene(s), comprising an E2F responsive transcriptional nucleotide regulatory site inserted into or in place of an endogenous adenoviral promoter that normally controls

the expression of said early gene(s) such that the endogenous adenoviral promoter no longer regulates the expression of said adenoviral early gene(s).

28. A viral vector as described in claim 1 and further comprising more than one viral packaging sequence.

29. A viral vector as described in claim 28, wherein said viral vector is an adenoviral vector.

30. A viral vector as described in claim 29, wherein said adenoviral vector is of the R1 form.

31. A viral vector as described in claim 29, wherein said adenoviral vector is of the R2 form.

32. A viral vector as described in claim 29, wherein said adenoviral vector is of the R3 form.

33. A method for killing tumor cells, comprising contacting said tumor cells with a viral vector of claim 28.

34. A viral vector comprising more than one packaging sequence.

35. A viral vector as described in claim 34, wherein said viral vector is an adenoviral vector.

36. A method for killing tumor cells, comprising contacting said tumor cells with an adenoviral vector of claim 35.